when the Mantoux reaction proves negative. Disseminated histoplasmosis has been seen in Britain, and three recent examples have been notable for the long interval recorded between the patients' last visit abroad and the onset of symptoms. This period was 14 years in the case reported by Hutchison (1952), and 7 years in each of those reported by Locket *et al.* (1953) and Poles and Lavertine (1954). With the increase of world travel the systemic mycoses, which almost without exception are acquired by the respiratory route, require consideration more frequently in differential diagnosis. Although they produce widely varying *x*-ray appearances, most of which are identical with those of tuberculosis, they each have their own individuality. At some stage during the course of infection they may present radiological features which should suggest the diagnosis (Pierce, 1953).

Summary

An increasing interest in mycotic diseases has been clearly evident in Britain during the past five years. A change of emphasis is occurring towards investigative studies of the kind which have long been established in the study of bacterial infections. The taxonomy of the pathogenic fungi is now sufficiently well adapted for accurate comparative studies, and pathologists are therefore no longer discouraged by a subject confused by synonymy. Critical laboratory opinion is now forthcoming for the support of clinicians in their widening appreciation of the diseases due to fungi.

Trichophyton rubrum infections of the skin and *Aspergillus fumigatus* infections of the lungs present difficult problems and are being recognized with greater frequency than in the past. The more unusual forms of torulosis have received study, and the subcutaneous and systemic mycotic diseases require consideration more often now that world travel is easier.

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HISTOPLASMOSIS CONTRACTED IN BRITAIN

A CASE OF HISTOPLASMIC LYMPHADENITIS FOLLOWING CLINICAL RECOVERY FROM SARCOIDOSIS

BY

W. St. C. SYMMERS, M.D., M.R.C.P.

Charing Cross Hospital and Medical School, London

[WITH SPECIAL PLATE]

The case described in this paper is believed to be the first mycologically proved case of histoplasmosis in which the infection was undoubtedly acquired in Britain. The characteristic causative organism, *Histoplasma capsulatum*, was isolated from a biopsy specimen. The patient had never been out of the British Isles before the infection developed. Four years earlier he had developed sarcoidosis; this appeared to have subsided completely a year before the mycotic infection presented as a localized lymphadenitis.

Histoplasmosis has seldom been recognized in this country (see below), where it is looked upon as an exotic disease and consequently has attracted little attention. A brief account of it may therefore be helpful as an introduction to the case report which follows. Fuller descriptions are accessible in the periodical literature (cf. Monroe and Kurung, 1953; Poles and Lavertine, 1954; Schwartz, 1954; Leigh and Thomas, 1955; Silverman *et al.*, 1955); the disease is dealt with scantily, when at all, in current general textbooks.

Clinical Features of Histoplasmosis

Histoplasmosis was discovered in 1905 by Darling (1906) in the Panama Canal Zone. No cases were found elsewhere until some 20 years later, when a case in Minnesota was reported by Riley and Watson (1926) and one from Honduras by Phelps and Mallory (1926); since then the disease has been recognized in many parts of the world.

For many years histoplasmosis was thought to be both rare and mortal; since the introduction of a specific skin test for sensitivity to histoplasmin (cf. Palmer, 1945) it has been realized that fatal infections are in fact exceptional. The histoplasmin test has helped to define large areas, particularly in the United States of America, where histoplasmosis is endemic; a high proportion of the population of these areas has passed through a clinically silent infection, as judged by the demonstration of sensitivity to histoplasmin—a circumstance which has its parallel in the comparable response to infection by the tubercle bacillus. A very large majority of subclinical histoplasmic infections occur in the lungs, where the calcified healed foci may present a striking radiological picture. When histoplasmosis does cause symptoms the clinical picture can be remarkably diverse—overt histoplasmosis has been appropriately described as a disease of protean clinical manifestations (Schwartz, 1954), for no organ is immune from colonization by the fungus.

Pulmonary involvement is among the commonest causes of clinical illness in histoplasmosis, just as it is the commonest form of subclinical infection. Many varieties of acute and chronic pulmonary lesions occur (Monroe and Kurung, 1953; Schwartz, 1954). Radiologically these lesions can mimic any form of pulmonary tuberculosis; diagnosis between pulmonary histoplasmosis and tuberculosis depends upon the bacteriological findings, supported by the results of skin tests with histoplasmin and tuberculin, and possibly by serological investigations. Occasional cases of combined tuberculous and histoplasmic infections have been reported. Some cases of pulmonary histoplasmosis present

as tuberculoma-like lesions which may simulate peripheral neoplasms (Zimmerman, 1954). The lesions in the lungs may heal or may remain active for many years; the infection may remain localized to the lungs or it may become disseminated in the lymphatic and blood streams, setting up fresh lesions anywhere in the body.

Both the self-limiting and the progressive forms of histoplasmosis may present as single or multiple granulomatous or ulcerative lesions of the upper respiratory tract, throat, mouth, or skin. The cutaneous lesions, like those of cryptococcal infection, may simulate rodent ulcers (Symmers, 1953, 1956). The clinical picture may be dominated by adrenocortical deficiency due to destruction of the adrenals by the infective process; acute adrenal insufficiency may occur unexpectedly in any patient with active histoplasmosis—for example, after surgical operations—unless the possibility of adrenal involvement is remembered (Crispell *et al.*, 1956). In other cases lymphadenopathy and hepatosplenomegaly, alone or in combination, may be the only findings, or there may be nothing more than vague malaise. Bone-marrow involvement is usual in cases of disseminated infection and may lead to anaemia, leucopenia, or purpura. Localized destructive lesions of bones and joints are rare (Key and Large, 1942). Histoplasmic meningo-encephalitis (Sprofkin *et al.*, 1955) and endocarditis (Beamer *et al.*, 1945) have been recorded.

Cytology

An interesting feature of some cases of the serious disseminated form of histoplasmosis is the predilection of the fungus for the cells of the so-called reticulo-endothelial system. In these cases the macrophages throughout the body may be filled with such great numbers of organisms, in the virtual absence of extracellular organisms, that it was even proposed that the disease should be described as "cytomycosis" (DeMonbreun, 1934). It is still uncertain whether this phenomenon is the result of active parasitic invasion of these cells or of brisk phagocytosis. The intracellular parasites are finely illustrated by photographs, reproduced by Payling Wright (1953), of preparations from a Southern Rhodesian case which came to necropsy in England (Cunningham and Garrod, 1950; Murray and Brandt, 1951—Case 3). However, histoplasmosis is by no means always associated with this type of systematized intracellular parasitization; a tuberculoid granulomatous reaction is characteristic of some cases, and in such lesions the parasites are usually found in foreign-body giant cells and may be scanty.

Mycology

Darling (1906) discovered histoplasmosis when he was actually looking for the organism which Leishman (1903) and Donovan (1903) had then just recently described independently as the cause of Dum-Dum fever, or kala-azar. Darling examined every enlarged spleen which he found at necropsy in Panama, and, although he found no leishmaniae at this time,* he collected three cases in which an encapsulated intracellular organism was present. He believed that this organism was a protozoon, and he gave it the name by which it is now generally known. Da Rocha-Lima (1913) drew attention to the morphological resemblance between Darling's *Histoplasma capsulatum* and *Cryptococcus farciminosus* (now commonly known as *Histoplasma farciminosum*), the causative organism of one form of epizootic equine lymphangitis; he suggested that *H. capsulatum* might belong to the fungal group of *Blastomyces*. The fungal nature of this organism was proved when DeMonbreun (1934) succeeded in cultivating it. *H. capsulatum* grows in two forms on culture media, a yeast-like growth developing at 37° C. and a mycelial growth at room temperature (cf. Conant, 1948; Conant *et al.*, 1954). Although the yeast-like phase seems to be the more pathogenic, both forms cause the disease when inoculated into animals. In each case it is the yeast-like form which develops in the tissues; the mycelial form has been found in naturally or experimentally infected tissues only as an extraordinarily rare phenomenon (Moore, 1955).

It is not certain whether all cases of human histoplasmosis are caused by a single type of histoplasma. Dubois *et al.* (1952) have suggested that at least some cases of the disease occurring in Africa are caused by an organism which they have named *Histoplasma duboisii*, and which differs from the usual strains of *H. capsulatum* in the presence of uncommonly large yeast-like forms in infected tissues. These large forms measure about 13 by 10 μ, while the yeast-like form of *H. capsulatum* measures about 3–4 by 2 μ. Such a large-cell strain was present in the skin lesions of Robb-Smith's (1943) case (mentioned by Duncan, 1945, 1946–7), in which the infection was probably contracted in West Africa, and also in my two cases in Nigerians (Symmers, 1956). Duncan (1946–7) also suggested that the large-cell strain might be a species or variety different from *H. capsulatum*. It should be noted that large yeast-like forms have been observed in exceptional American cases (Moore, 1955), although usually only in necrotic lesions (Binford, 1955; Silverman *et al.*, 1955). Similar large forms developed in tissue explants from organs infected with *H. capsulatum* which had been isolated from an American case (Schwarz, 1953). The significance of these atypical American observations is not clear, but Moore (1955) cited them in his rejection of the existence of *H. duboisii* as a distinct species. Drouhet and Schwarz (1956) also felt that there is not enough evidence to establish the African strains as a species different from *H. capsulatum*.

Some Epidemiological Factors

Histoplasmosis occurs as a natural infection in many species of domesticated and wild animals, including rats and house-mice (for references see Schwartz, 1954). Although there is no evidence of case-to-case transfer of infection in man, there is experimental evidence that infections can be transmitted naturally from dog to dog (Prior and Cole, 1951). It is possible that human infection has resulted from contact with infected animals in cases where the disease in man has occurred in households where pets or house-mice are also infected (Pará, 1946; Olson *et al.*, 1947); however, it may well be that in such cases man and beast have been infected from a common source, such as dust. Spread of the infection by vectors has not been observed. Ticks can be infected experimentally by feeding on blood from infected dogs, but there is still no evidence that they can then transmit the fungi to other animals (Olson *et al.*, 1947).

H. capsulatum has been isolated repeatedly from soil and dust (for references see Grayston and Furcolow, 1953). In some instances small local epidemics of acute pulmonary histoplasmosis, usually non-fatal, have been traced to exposure to infected dust, such as in cleaning out or demolishing derelict buildings, particularly on farms. Exploring caves and playing in hollow trees have been linked to other outbreaks. Sawdust, decaying wood, and excreta of animals and birds have been incriminated as the source of infection in some outbreaks; they possibly provide the moist environment necessary for growth of the fungus, while yet allowing the infective material to dry out enough to be carried on air currents, when disturbed, and so to enter the lungs of those exposed.

Incidence

Although only about 300 cases of histoplasmosis in which the diagnosis was confirmed by cultivation of the organism or by its histological demonstration have been published, the incidence of the infection is enormously higher than this figure suggests, if one judges it by the high proportion of individuals with positive histoplasmin reactions in endemic areas. Histoplasmosis is known to occur in many parts of

*In view of Darling's (1906) discovery of histoplasmosis while looking for cases of leishmaniasis in Panama, it is interesting to note that, later, he was in fact the first to recognize and prove the occurrence of leishmaniasis ("oriental sore") in that country (Darling, 1911).

the world; its geographical distribution is far from completely worked out, and may prove to be world-wide. Its incidence varies greatly in those areas where it has been recognized. In some areas only sporadic cases have been found, and histoplasmin-sensitivity surveys show a low incidence of positive reactors. Elsewhere, as in parts of the great endemic areas of the Mississippi, Missouri, and Ohio valleys, as many as 80 or more persons in every hundred show evidence of past subclinical infection in the form of a positive histoplasmin skin reaction (cf. Schwartz, 1954), and according to Silverman *et al.* (1955) it has been estimated that 20 to 30 million people in the U.S.A. have histoplasmic infection. Outside the United States the infection is said to be most prevalent in Mexico and Central America; an increasing number of cases is being recognized in Canada, South America, Africa, the East Indies, the Pacific islands, and Australasia. Sporadic cases have been found in countries bordering the Mediterranean, and the few European cases appear to have been confined to that area.

Histoplasmosis Recognized in Britain

In an earlier paper (Symmers, 1953) reference was made to eleven occasions on which the diagnosis of histoplasmosis was suggested by various workers in Britain; this series included two then unpublished cases of my own which have now been reported (Symmers, 1956). Three more case reports have been published in this country, making, with the case recorded in the present paper, a total of 15 cases diagnosed here as histoplasmosis. This diagnosis appears to have been adequately substantiated in 13 of the cases, in six of which the causative organism was isolated by culture. These 13 cases are listed in the Table.

In Limerick's (1951) two cases the evidence is insufficient to warrant the diagnosis of histoplasmosis. The only evidence in his first case was that *H. capsulatum* was said to have been found on microscopical examination of pus obtained on incision of an abscess which developed in the right iliac fossa following interval appendicectomy; his second case was given only passing mention as a case of "histoplasmosis of lungs following a visit to Ireland, where this infection is known to occur—possibly spread from the U.S.A." Limerick's first patient had never been outside England; he did not say whether his second patient had been farther afield than Ireland. Apart from Limerick's case and the one described below, in all cases in which histoplasmosis has been diagnosed in Britain the patient is known to have spent some time abroad in a country where histoplasmosis occurs. In view of Limerick's (1951) statement that histoplasmosis occurs in Ireland, it may be noted that there does not appear to be any published record that such is the case; the only histoplasmin-sensitivity survey which has been reported gave negative results (McWeeney *et al.*, 1946). I am obliged to Dr. J. A. D. Deeny, Chief Medical Adviser to the Department of Health of the Republic of Ireland, and to Dr. F. F. Main, Chief Medical Officer of the Ministry of Health and Local Government of Northern Ireland, for the information that they know of no cases of histoplasmosis occurring in Ireland.

The case of Poles and Lavertine (1954) is of particular interest because of their suggestion that their patient, a post-office clerk, acquired the infection in England about eight months before his death in 1951. Their diagnosis was based on the presence of morphologically typical histoplasmas in sections of tissues obtained at biopsy and necropsy; histoplasmin tests were negative and attempts to cultivate the organism failed. The patient had been in France in 1939, in Nigeria (where histoplasmosis is known to occur: Clarke *et al.*, 1953) in 1942, and in Burma in 1944; while overseas he had no illness except "jungle sores." Not enough is known about the natural history of histoplasmosis to exclude the possibility that the infection could have remained dormant for several years. Poles and Lavertine (1954) mentioned a personal communication from Furcolow, in which he stated his belief that relapses of histoplasmosis do not occur, but commented that the

*Table Showing Cases of Histoplasmosis Recognized in Britain**

Authors (Chronological Order)	Type of Disease	Cultivation of *H. capsulatum*	Histological Finding of Organisms	Histoplasmin Sensitivity	Patient's Age at Time of Diagnosis (Years)	Year of Diagnosis	Patient's Residential History†
Derry *et al.*, 1942	Fatal disseminated	Positive	Typical	No data available	30	1940	India, 1932–6. Sudan, 1936–7. Britain, 1937–9. France, 1939–40 (about 4 months). Britain, 1940
Robb-Smith, 1943 (Case mentioned by Duncan, 1945, 1946–7)‡	Cutaneous (benign). (History of sputum-positive pulmonary tuberculosis, 1940)	,,	Large-cell type	Negative at time of re-examination in 1948, when skin lesions had disappeared	64	1943	*Born in Australia.* Australia, 1879–1911; West Africa, 1911–14; Burma, 1914–30; Britain, 1930–3; Gold Coast, 1933–40. Britain, 1940 onwards
Arblaster, 1950 ..	Pulmonary (? chronic active; ? healed)	Negative	No data available	Positive	36	1949	Canada (Montreal and Great Lakes), 1931–7. Britain, 1937 onwards
Crofton, 1950: Case 1	Pulmonary (healed)	No data available	,, ,,	,,	43	No data available	30 years before diagnosis spent 3 years in Ontario, with 2 short visits to Michigan. Britain from then onwards
Crofton, 1950: Case 2	,, ,,	,, ,,	,, ,,	,,	41	1950	Southern and central States of U.S.A., 1929–38. Britain, 1938 onwards
Hutchison, 1952	Laryngeal (benign)	Negative	Typical	No data available	72	1948	Spent 30 years in India, with short periods in Malaya. Britain, 1934 onwards
Sakula, 1953 ..	Pulmonary (healed)	,,	No data available	Positive	36	1951	*Born in Kentucky.* Kentucky, 12 years; Florida, 18 years; South Carolina, 3 years. Britain, 1951
Locket *et al.*, 1953	Fatal disseminated	Positive	Typical	Negative	32	1952	War service, 1939–45: mostly in Egypt, with short visits to Tobruk, India, S. Africa, and in Near East. Britain, 1945 onwards
Poles and Lavertine, 1954	,, ,,	Negative	,,	,,	45	1951	France, 1939; Nigeria, 1942; Burma, 1944. Britain, 1945 onwards
Leigh and Thomas, 1955	Pulmonary (healed)	,,	No data available	Positive	42	1955	*Born in Jamaica.* Jamaica until 1944; Ohio, 1944–7; New Jersey, Florida, New York, 1947–9; Jamaica, 1949–51. Britain, 1951 onwards
Symmers, 1956 (case in this paper)	Lymphadenitis	Positive	Typical	,,	46	1955	*Never out of British Isles*
Symmers, 1956: Case 1	Cutaneous (benign)	,,	Large-cell type	Negative	30	1953	*Born in Nigeria.* Nigeria until 1951. Britain, 1951–4
Symmers, 1956: Case 2	,, ,,	,,	,, ,,	Positive	24	1953	*Born in Nigeria.* Nigeria until 1952. Britain, 1952 onwards

* The case demonstrated in London by Cunningham and Garrod (1950), and reported by Murray and Brandt (1951—Case 3), is not included. The patient, a boy, contracted histoplasmosis while living in Southern Rhodesia; the diagnosis was made in South Africa; he died soon after arriving in England. This is the case mentioned by Locket *et al.* (1953) at the end of their paper (Atkinson, 1953).

† Unless otherwise stated, the available data suggest that the patients were born in Britain and lived there except during the times mentioned.

‡ This case was shown before the Section of Dermatology, Royal Society of Medicine, London, on January 21, 1943 (Carleton, 1942–3).

evidence for this is not yet conclusive. Observations such as have been made by Monroe and Kurung (1953) and others suggest, in fact, that the infection may sometimes lie dormant for years and then break out again. If it is eventually shown that histoplasmic infection does not exist in a dormant state, the case of Locket *et al.* (1953), and possibly that of Derry *et al.* (1942), as well as that of Poles and Lavertine (1954), will have to be accepted as indigenous British infections. The case which is reported here shows that the causative organism can be acquired in this country.

CASE REPORT:

Traumatic Siliceous Granuloma of Skin; Sarcoidosis; Histoplasmic Lymphadenitis

A man, born in 1909, fell and cut his forehead on a path of splintered flint near the Gobbins, County Antrim, when on holiday in 1936. The wound, about 2 cm. long, healed rapidly without suturing. In April, 1950, the scar became livid, and indurated, forming a slowly growing, smooth linear swelling (about 2×0.5 cm.). It was excised in August, 1950; sections showed a typical siliceous granuloma formed of tubercle-like structures of sarcoid type around irregular fragments of birefringent yellow or blackish material which withstood micro-incineration at 660° C. for ninety minutes.

In August, 1951, the patient consulted his doctor because of increasing enlargement of the lymph nodes in his neck, armpits, and groins. He had first noticed these nodes about six months earlier. He had no other symptoms. Examination showed generalized symmetrical enlargement of the superficial lymph nodes: none was larger than 1.5 cm. in longest dimension. The nodes were discrete, firm, and mobile. There was no other clinical abnormality. His skin, the scar following excision of the siliceous granuloma, and the scars of old superficial wounds on the knees and hands were healthy.

Investigations.—Radiograph of chest: sparse "woolly" miliary shadows in both lungs, mainly in the middle zones; pronounced enlargement of hilar shadows. Mantoux reaction negative with 0.2 ml. of 1 in 1,000 old tuberculin, weakly positive with 1 in 100. Wassermann and Kahn tests negative. Serum albumin 4.4 g., globulin 4.0 g. per 100 ml. Haematological findings normal. Biopsy of an epitrochlear lymph node (August 12) showed a picture consistent with sarcoidosis (Special Plate, Fig. 1). The node was uniformly and closely studded with rounded aggregates of epithelioid histiocytes. In places the aggregates merged together, maintaining their rounded contour so that the constituent aggregates remained identifiable. No giant cells were seen; there was no necrosis.

Progress.—No treatment was given. The patient continued his administrative occupation without interruption. The lymphadenopathy subsided completely within the following year and the radiological changes in the lungs slowly resolved. In April, 1954, he felt perfectly well; chest radiographs were completely normal; Mantoux reaction positive (1 in 1,000); serum albumin 4.8 g., globulin 2.6 g.; erythrocyte sedimentation rate 3 mm. in one hour (Westergren).

In May, 1955, he noticed two small, mobile lymph nodes above the medial end of the left clavicle. Clinical examination showed no other abnormality. At the patient's request, as he was about to go overseas, one of the nodes was excised (May 6).

Histology and Mycology.—Section of the lymph node excised in May, 1955, showed a granulomatous lymphadenitis quite different from that in the biopsy of August, 1951. There was patchy replacement of the lymphoid tissue by epithelioid histiocytes, without formation of rounded aggregates; moreover, in striking contrast to the earlier biopsy, every field contained many large multinucleated giant cells (Plate, Fig. 2), in which many organisms resembling *H. capsulatum* were present (Plate, Fig. 3). The organisms were exclusively intracellular, mostly in giant cells, although occasionally a single organism was seen in a simple histiocyte. Many of the organisms stained faintly and appeared to be fragmentary or undergoing lysis. The siliceous granuloma of 1950 and the lymph node excised in 1951 were now re-examined; serial sections were cut at different levels in the paraffin blocks and stained by a variety of methods, including Gram, Gridley, and periodic-acid–Schiff stains; no organisms were found in either of these specimens.

The second supraclavicular node was excised (May 25, 1955) and cultures were prepared on blood-agar and on Sabouraud's medium at room temperature and at 37° C.; the pathologist did not keep the specimen for histological examination, a mistake which is the more regrettable as the paraffin block of the specimen of May 6 was lost while in transit to London. The cultures yielded an abundant pure growth of *H. capsulatum*. The yeast-like phase grew up well, within 48 hours at 37° C., as cream-coloured, smooth colonies of oval, budding cells 1 to 4 μ in diameter. Growth was slower at room temperature, but on the sixth day small, whitish, cottony colonies of fine, branching, septate mycelium were present; the mycelium carried smooth, rounded conidia, about 3 μ in diameter, on short lateral branches. After 16 days at room temperature the colonies had become ochre-coloured, and numerous characteristic thick-walled tuberculate chlamydospores, about 10 μ in diameter, had developed.

The laboratory where the case was being investigated was taken over by another pathologist at this time. He at once destroyed all the cultures and the animals which had been inoculated by his colleague, under the impression that *H. capsulatum* is particularly dangerous to laboratory workers. It is true that laboratory infections with *H. capsulatum* have occurred (Furcolow *et al.*, 1952; Nilzén and Paldrok, 1953; Spicknall *et al.*, 1956); the risk seems to be slight, however, and the opinion of Raphael and Schwarz (1953) that "reasonable precautions will protect the laboratory worker against Histoplasma infections" is generally accepted; moreover, laboratory infections usually result in the localized pulmonary form of the disease, which has a good prognosis, in contrast to the lethal but comparatively uncommon disseminated form.

The patient took up a post abroad before detailed investigations could be completed; at that time (May, 1955) there were no symptoms or abnormal physical signs. The chest radiograph was normal. A skin test (intradermal injection of 0.1 ml. of 1 in 1,000 histoplasmin) gave a strongly positive reaction, producing a 3-cm. circle of erythema with a central zone of induration, 1.5 cm. across, in 48 hours. When last heard from (September, 1956) he reported excellent health, with no symptoms.

Until leaving England in 1955 this patient had never been out of the British Isles. None of his household had ever been abroad, none reacted to intradermal histoplasmin, and there was no family history relevant to his illness. His work brought him into frequent contact with American visitors; this is probably without significance, as there is no evidence that the infection is transmitted from person to person. He did not handle stores or packings from abroad. His hobbies and recreations did not expose him to any environment which has been incriminated as a source of infection. He lived in the country, but had no interest in gardening or farming; he kept no pets and he had no contact with livestock. Attempts to isolate *Histoplasma* from the soil of his garden and from various outhouses and wood-piles were fruitless.

Comment

This patient's initial illness (sarcoidosis) ran a benign course over about three years. All its manifestations had disappeared by April, 1954, a year before the histoplasmic lymphadenitis developed. The growth of a siliceous granuloma in a 14-year-old scar about six months before he noticed the generalized lymphadenopathy is interesting; this lesion was a typical example of Shattock's (1916–17) "pseudotuberculoma silicoticum." It is only recently that the occasional relationship between the appearance of this delayed and typically sarcoid tissue reaction around some

foreign bodies and the development of the manifestations of systemic sarcoidosis has been recognized (Refvem, 1954; Löfgren *et al.*, 1955). There is no reason to presume any relationship between the old injury in this case and the eventual development of the fungal infection.

It is unlikely that the original illness, believed to be sarcoidosis, was in fact a manifestation of histoplasmosis. The absence of symptoms, the apparently complete recovery, the character of the radiological changes in the lungs and their disappearance without calcification, the clear-cut histological picture of sarcoidosis, and the failure to find parasites in the original biopsy and in the siliceous granuloma are all features which favour the diagnosis of sarcoidosis. However, none of these observations is incompatible with the diagnosis of histoplasmosis, and therefore the latter cannot be altogether excluded in considering this earlier phase in the patient's history.

There does not appear to be any record of histoplasmosis occurring in a patient who at that or any other time showed evidence of any illness which could reasonably be interpreted as sarcoidosis. There have been a few cases in which histoplasmosis mimicked sarcoidosis histologically, but none of these showed anything like the apparently clear picture of sarcoidosis in the case described here (Reimann and Price, 1949; Pinkerton and Iverson, 1952; Israel *et al.*, 1952; Binford, 1955; Crispell *et al.*, 1956).

The association of sarcoidosis with other fungal infections, particularly torulosis, is discussed briefly elsewhere (Plummer *et al.*).

Summary

A case of histoplasmosis is described. The only manifestations of the infection have been enlargement of two cervical lymph nodes and a positive histoplasmin skin reaction. Fungi were found in sections of one of the lymph nodes. The diagnosis was proved by the isolation of *H. capsulatum* in cultures from the second node. The patient is without symptoms 16 months after the mycotic lymphadenitis appeared.

The patient had never been out of the British Isles before he developed histoplasmosis. His case is believed to be the first unequivocal instance of mycologically proved histoplasmosis in which the infection was contracted in Britain.

He had previously had sarcoidosis, the course of which was benign. The first manifestation of sarcoidosis was probably the development of a siliceous granuloma at the site of an old injury.

I am much obliged to Mr. R. J. Lunnon, A.I.B.P., A.R.P.S., Department of Medical Photography, St. John's Hospital for Diseases of the Skin, London, for his kindness in preparing the photomicrographs.

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LOCALIZED CUTANEOUS HISTOPLASMOSIS

BY

W. St. C. SYMMERS, M.D., M.R.C.P.

Charing Cross Hospital and Medical School, London

Two cases of localized cutaneous histoplasmosis, confirmed by isolating *Histoplasma capsulatum*, are described in this communication. Both patients are Nigerians. The diagnosis was made while they were living in England; it is clear that the infection was acquired before they came here. Their cases were referred to as "unpublished observations" in an earlier paper (Symmers, 1953), and were listed in a more recent paper (Symmers, 1956) in a table of 13 acceptable cases of histoplasmosis which have been recognized in this country. A mycologically proved histoplasmic infection has only once been reported in a patient who had never been out of Britain (Symmers, 1956).

Case 1

A Nigerian man, aged about 28, came to England at the end of 1951. He had not been away from Nigeria before. His health had always been good. He travelled to England by sea from Lagos, where he lived, calling ashore at Accra on the Gold Coast, Freetown in Sierra Leone, and Bathurst in Gambia. Two days after sailing from Bathurst he developed a pustule on one cheek: thinking that this might be due to a bite by a tumbu-fly (*Condylobia anthropophaga*) he incised it carefully with a sterile scalpel and evacuated its purulent contents—no larva was present. The lesion healed over quickly, but a little painless nodule remained at its

W. ST. C. SYMMERS: HISTOPLASMOSIS CONTRACTED IN BRITAIN

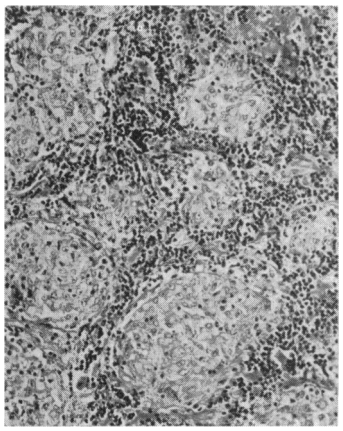

FIG. 1. — Lymph-node biopsy (August, 1951): sarcoidosis. The absence of multinucleated giant cells is noteworthy. (Haematoxylin and eosin. ×200.)

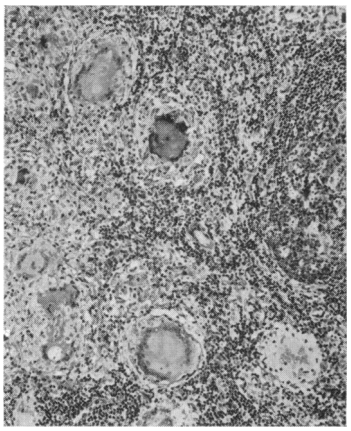

FIG. 2.—Lymph-node biopsy (May, 1955): granulomatous lymphadenitis, with many multinucleated giant cells. Part of germinal centre of a follicle seen at right of picture. (Haematoxylin and eosin. ×150.)

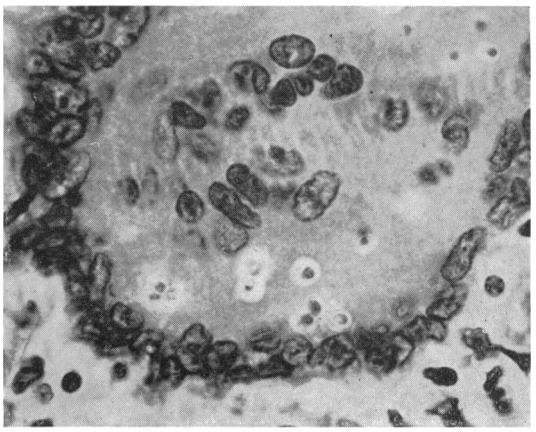

FIG. 3.—Part of giant cell from same section as Fig. 2. Fourteen histoplasmas in cytoplasm; some lie in so-called "digestion vacuoles"; double-contoured capsule of some organisms clearly seen. (Haematoxylin and eosin. ×925.)

G. A. ROSE: RENAL TUBULAR OSTEOMALACIA

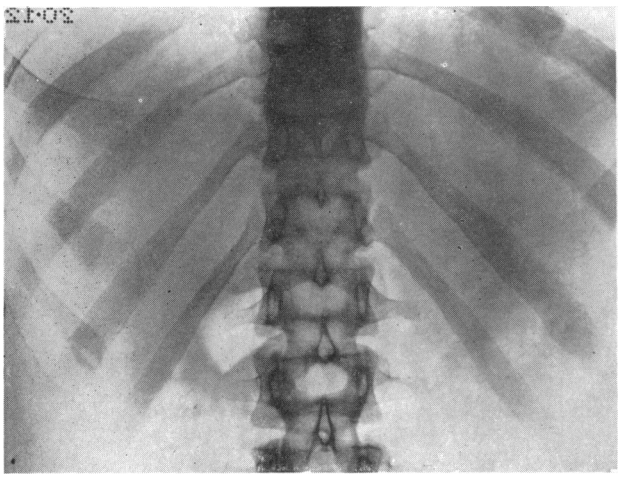

FIG. 1.—Radiograph of lower ribs on December 20, 1954, showing Looser's zones in ribs R 10 and 11 and L 11. Bones otherwise well calcified and apparently normal.

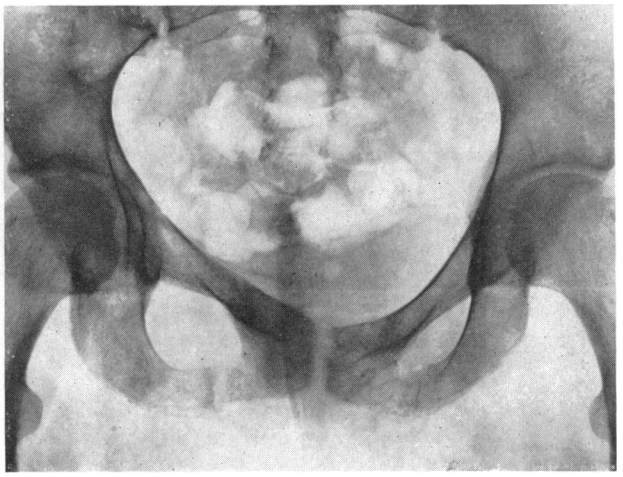

FIG. 2.—Radiograph of pelvis on December 20, 1954, showing Looser's zones of both ischial rami.

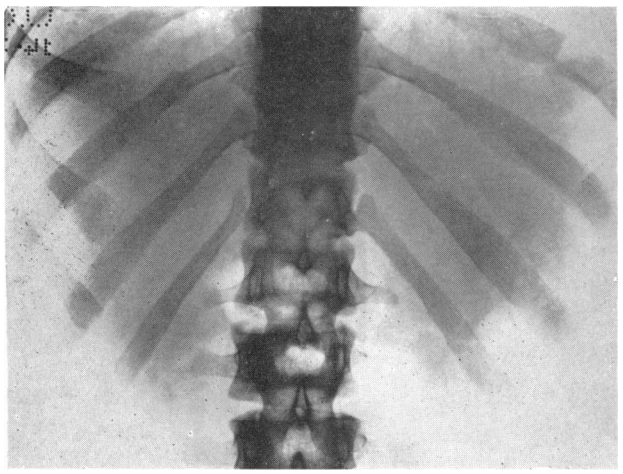

FIG. 3.—Radiograph of lower ribs on March 14, 1955, showing laying down of callus and calcification of Looser's zones after treatment for ten weeks.

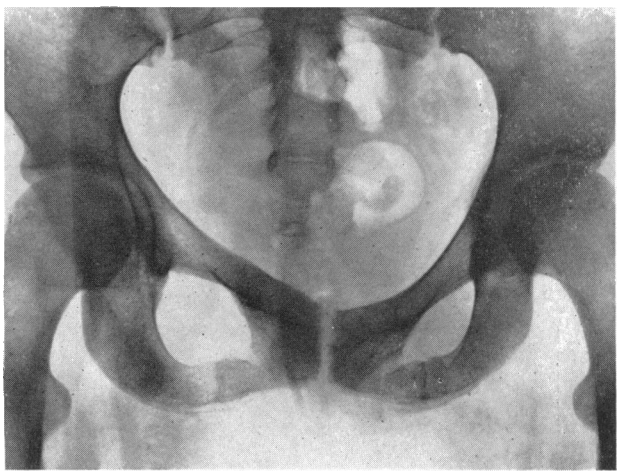

FIG. 4.—Radiograph of pelvis on March 14, 1955, also showing calcification of Looser's zones after treatment.